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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,253	10/24/2001	Linda G. Lee	4478D2 US	3709

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,253	LEE ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-105* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-105* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 70-105 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term "aminopyridinium group" is unclear. The term is not defined in the specification. It is of particular importance because, as applicants have correctly pointed out, this is the feature which distinguishes these claims from the previously applied prior art. There are four ambiguities: a) Does the group have to be attached via the pyridinium N? It is noted that all species have this feature. Could it be –NH-Pyridinium? Given that the moiety is permitted to be substituted, could it be attached via its substituent? That is, could it be e.g. $-CH_2$-(aminopyridinium), where the methyl group is attached to either the amino N or to the ring? b) Does the amino have to be attached directly to the ring? It is noted that all species have this feature. Could it be –Pyridinium-J-amino, where J is a linker of some sort? Could the amino be present in the counterion to the pyridinium (e.g. the carbamate anion)? c) What qualifies as a "substituted" amino? For example, groups such as the carboxamido

(e.g. acetamido), sulfonamido (e.g. methanesulfonamido), nitro, isocyano, nitrosyl, hydrazino, azido, diazonium ($-N_2^+$) and quaternary ammonium (e.g. $-N(methyl)_3^+$) among monovalent choices and diazo ($=N_2$) or imino (e.g.=NH, where the = is either one double bond, or two single bonds to adjacent carbons to form a three membered C_2N ring) for divalent choices are not normally thought of, or named, as being substituted amino but could be viewed as a substituted amino with a sufficiently broad definition of what is a substituent. Which of these are and which are not included, and how would one of ordinary skill in the art know this? d) Does the term "pyridinium" include fused choices, such as pyrrolopyridium, quinolinium, isoquinolinium, acridinium, etc.? Again, these might or might not be considered as falling within the "pyridinium" claim language. In this regard the paragraph bridging pages 2-3 of the specification, and the following paragraph are noted. This is not in the form of a definition. For example, while this says that the amino group "is located at the 4-position", there is no such limitation in the claim. The PTO does not read unexpressed limitations or characteristics into the claims, *In re Kebrich*, 96 USPQ 411, 413. Similar is *In re Winkhaus*, 188 USPQ 129: "We will not read into claims ... limitations from the specification." Note also *In re Prater*, 162 USPQ 541, 550; *Storage Technology Corp. v. Cisco Systems Inc.*, 66 USPQ2d 1545; *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 7 USPQ2d 1129 and *Intervet Am., Inc v. Kee-Vet Labs., Inc.*, 12 USPQ2d 1474, 1476.

2. The terms "common analog" (e.g. second line of B definition in claim 70) or "analog" (e.g. last and first lines of claim 70; claim 71, line 1) are indefinite. There is no way to know what is an analog and what is not, or to know what is an uncommon as

opposed to a common analog. The material on specification pages 12-14 for nucleoside and nucleotide analogs is noted, but this says that an analog is an analog, and then gives some examples, but that does not make it clear what the actual boundary of the term is. What else is there other than the examples given?

3. Claims 70 and 105 for example refer to "ortho" – but ortho to what? The xanthene? The aminopyridinium? The substituted thio? Since the phenyl group has 4 substituents, the carboxy almost has to be ortho to something.
4. The term "C9" is unclear. The 9-position will appear at different places depending on how many rings are fused onto the rhodamine core.
5. The term "linker" in claim 70 and elsewhere is indefinite. It states where something is, but not what it is.
6. Substituted (in the substituents on the C9-phenyl and elsewhere) with what?
7. In the definition of R70, "template-directed polymerization" of what? RNA? activated mononucleotides? Acryloylnucleosides? Any nucleoside 5'-triphosphates? Its impossible to tell just what the scope of this is.
8. Further, which types of polymerases are being referred to? There are many, many different types. There's no practical way to determine that a given moiety does not fall within R70 or R71. Points 6 and 7 affect claims 98-100 as well because of how the terms in these claims are defined in the specification.
9. The term "alkyl" has been rendered indefinite by the specification. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947) and MPEP 2173.01. The meanings quoted by applicants on

page 14 of the specification are not the usual meaning at all. Alkyl is a group of the formula $-C_nH_{2n+1}$, as is set forth in such sources as Hack's Chemical Dictionary and Hawley's Condensed Chemical Dictionary, or any textbook of organic chemistry. As such it cannot be unsaturated or have rings either for that matter.

10. The term "heteroalkyl" is indefinite. It appears to have no meaning at all, since anything at all, organic or inorganic, can be a heteroalkyl. It begins with a hydrocarbon which can be cyclic or non-cyclic, and which can be saturated or unsaturated. In heteroalkyl, one or more atoms can be replaced with any other atom, so that any substituent qualifies as a heteroalkyl. Thus, the intended meaning is unclear. If applicants disagree, they are invited to present a moiety which is not a heteroalkyl.

11. The definition of L' and the definition of R24-R24' combined have both heteroalkyldiyl and heteroalkyleno. It is not clear what the function of the latter term is because, if the text of the specification, which is not a model of clarity, is understood, the former term completely embraces the latter. If that is true, then why is the heteroalkyleno present – how does it define the invention? If it is not true, then what is a heteroalkyleno but not a heteroalkyldiyl? Likewise for "alkyldiyl or alkyleno" at claim 74, line 3 and elsewhere.

12. Similarly, it is not clear why Y-3 and Y-4 appear in claim 72. These both appear to be already embraced by Y-2. Likewise in claim 83.

13. The meaning of the dashed bond present in Y-2 and Y-4 is unclear. It could mean a) an optional double bond or b) an aromatic bond only to exist when the 4 surrounding variables combine to form an aromatic ring. Clarification is needed.

Note that there is no provision made for two variables disappearing if this is just a regular double bond.

14. Terms starting with "heteroalkyl" that have carbon counts are not clear. Is this the total number of carbons before or after the replacement has occurred? That is would –O- qualify as a C1 heteroalkyldiyl because it started as a C1 group, or would it not qualify because it in fact has zero carbons? Would hexyloxy count as a C6 heteroalkyl because it has 6 carbons, or not count because it started with 7 before the substitution occurred? As the claim is literally written, it would be the former in both cases, but that might not be applicants' intention.

15. The term "aryl" has been rendered indefinite by a specification (page 20) which includes as a choice "penta-2,4-diene". It is not seen how this group could possibly meet the definition of aryl. It is not even a ring.

16. The was claim 73 is written, it is improperly dependent on claim 72 because it does not further limit. As worded, it does not require that R2 be combined, it just says what it is when it is combined, but that definition is the same as appears in claim 72.

17. Claim 74, line 6 has R1 combined with R2. However, claim 72 on which it depends makes no provision for combining these two variables. R1 is not permitted to combine with anything.

18. In claim 78, the variable R9 has no definition.

19. The reference to the "C4 atom" at next to last line of claim 83 is not correct for the last three structures, since the indicated position is a different one. Likewise claim 91.

20. The last two choices in claim 87 are not provided for in claim 82, since these are not aryl but heteroaryl.

21. In claim 91, choice Y-22c does not have a dashed line; the actual line looks to be solid and this needs to be redrawn.

22. Claims 78 and 92 need to end in a period.

23. Claim 94 is unclear. A compound cannot comprise another compound. A mixture, an adduct, a solvate, a complex, etc can comprise another compound, but a compound itself cannot. Judging from claim 96, applicants actually do not intend another molecule, but intend an additional moiety covalently attached to the rest of the molecule. Since the molecule is permitted pretty much unlimited substitution, this is not a problem per se, but the claim must be written to show that the cyanine, etc., is a substituent. If, however, applicants intend more than just that option, the claim can set this forth, but at present, claims 94-95 in indefinite in this regard.

Claims 70 –105 are rejected under 35 U.S.C. 112, paragraphs 1 and 2, as the claimed invention is not described, or is not described in such full, clear, and exact terms as to enable any person skilled in the art to make and use the same, and/or failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. Specifically:

The molecule is depicted in claim as having plus charges and possibly minus charges, but not necessarily in balance. A molecule without electrical neutrality is impossible to prepare and hence lacks enablement in terms of how to make, as such a thing cannot be made (paragraph 1). Note MPEP §2172.01: "A claim which omits matter disclosed to be essential to the invention as described in the specification or in

other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling. In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). See also MPEP §2164.08(c). Such essential matter may include missing elements ...". Here, the missing counterion is the missing element. On the other hand, if it was not the intention of applicants to claim such a non-neutral molecule, then the claim fails to set forth what applicants intend as their invention (paragraph 2). That is, it is not accurate because it is missing something. As stated in *In re Zletz*, 13 USPQ2d 1320, 1322, "An essential purpose of patent examination is to fashion claims that are precise, clear, correct and unambiguous."

Specifically, the compound is depicted as having one positive charge on the rhodamine, and one to three for the aminopyridiniums. Thus, the compound has 2-4 plus charges. Minus charges can arise when R72 is a phosphate ester, which can provide 1-3 of these, depending on the value of "a". In addition, there are two charged possibilities (SO_3^- and CO_2^-) for W1 and W2, and there is no specific upper limit to how many of these there are; there could be a dozen. It is not clear what is intended. It may be that there are intended associated anions or cations. However, the claim does not provide for them. It may be that applicants intend that the charges exactly cancel (i.e. the compounds are zwitterions), but again, there is no such requirement made. If applicants opt to fix this with anions or cations, care should be taken to use only ions such as have description in the specification.

US 6649769 is cited as closest prior art, as the column 9 description for the variables R17-R20 includes both the aminopyridinium and the substituted thio choices.

However, no examples are seen of their use, and hence there are no guidepost to a molecule with both of such substituents, and so no 35 USC 103 rejection is made.

Specification

The abstract is objected to as too vague. It fails to convey the essential feature of having the aminopyridinium and substituted thio substituents on the phenyl.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571)272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Berch
Primary Examiner
Art Unit 1624

9/10/04